57. The method of Claim 41, wherein the procaspase or caspase activity is increased.

58. The method of Claim 45, wherein the enhanced activity results from enhanced conversion of procaspase to caspase.

59. The method of Claim 45, wherein the enhanced activity results from enhanced oligomerization of the caspase.

60. The method of Claim 45, wherein the enhanced activity results from enhanced expression of procaspase or caspase.

61. The method of Claim 45, wherein the procaspase or caspase activity is prolonged.

62. The method of Claim 45, wherein the procaspase or caspase activity is increased.

63. A method of identifying an agent which enhances the activity of a caspase or procaspase expressed in immature thymocytes, or an active derivative or fragment thereof, wherein said caspase is necessary for apoptosis, comprising the steps of:

(a) contacting the caspase or procaspase, or an active derivative or fragment thereof, with biotin-DEVDamk in the presence of the agent; and

(b) identifying enhancement of caspase or procaspase activity.---

REMARKS

Prior to entry of this Amendment B, Claims 41 and 45 are pending in this application. No claim is allowed.

In this Amendment, Claims 41 and 45 have been amended, and new Claims 53-63 have been added. The amendment of the claims is for the purpose of more particularly pointing out the subject matter which Applicants regard as their invention, and for the purpose of expediting prosecution. The amendments should not be construed as agreement with or acquiescence to any of the pending rejections.

Support for the amendments and new claims can be found throughout the specification, the claims and the figures as originally filed. Specifically, support for the amendments to Claims

41 and 45 can be found at least in the specification at page 3, line 26. Support for new Claims 53 and 58 can be found at least in the specification at page 38, line 33. Support for new Claims 54 and 59 can be found at least in the specification at page 39, line 1. Support for new Claims 55 and 60 can be found at least in the specification at page 39, lines 4-5. Support for new Claims 56 and 61 can be found at least in the specification at page 39, line 18. Support for new Claims 57 and 62 can be found at least in the specification at page 39, line 19. Support for new Claim 63 can be found at least in the specification at page 53, line 25. No new matter has been added to the application by the amendments or by the addition of these new claims.

Rejection of Claims 41 and 45 Under 35 USC §112, Second Paragraph

Claims 41 and 45 stand rejected under 35 USC §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

The Examiner states at Page 2 of the Action that in the recitation of "enhanced caspase or procaspase", it is not clear if the enhance relates to the activity or expression or levels of the caspase or procaspase.

Claims 41 and 45 have been amended to more particularly point out that the agent enhances the activity of an isolated caspase or procaspase. Applicants believe that the claims, as amended, even more particularly point out and distinctly claim the subject matter of Applicants' invention. Therefore, it is respectfully requested that the rejection be reconsidered and withdrawn.

Rejection of Claims 41 and 45 under 35 USC §103(a)

Claims 41 and 45 stand rejected under 35 USC §103(a) as being unpatentable over Fearnhead *et al.*, "An Interleukin-1β-Converting Enzyme-like Protease is a Common Mediator of Apoptosis in Thymocytes", *FEBS Lett.*, 375: 283-288 (1995).

Specifically, the Examiner acknowledges at Page 3 that:

> Fearnhead et al do not teach methods to enhance the levels or activity of caspase or procaspase in the thymocytes or isolated and purified caspases expressed in immature thymocytes...

But then continues:

> ...Thus it would have been prima facie obvious to one of ordinary skill in the art at the time of the claimed invention to substitute in the cell lysate employed by Fearnhead et al other agents that might have the property of enhancing the apoptosis by enhancing the ICE-like proteases (or caspases), since one of ordinary skill in the art would not expect the thymocyte cell lysates not to contain the caspases.

Applicants specifically traverse the rejection on the grounds that Fearnhead *et al.* neither teach nor suggest a method of identifying an agent which enhances caspase or procaspase activity, nor a method of enhancing the activity of caspase or procaspase. Moreover, Claims 41 and 45 have been amended to more particularly point out that the caspase or procaspase is isolated, as suggested by the Examiner on page 4 of the Office Action. Therefore, reconsideration and withdrawal of the rejection are respectfully requested.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned at (781) 861-6240.

Respectfully submitted,

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